



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :

C07D 223/14, C07F 7/08, C07D 301/03,
C07B 53/00

A1

(11) International Publication Number:

WO 97/06147

(43) International Publication Date:

20 February 1997 (20.02.97)

(21) International Application Number: PCT/EP96/03551

(22) International Filing Date: 7 August 1996 (07.08.96)

(30) Priority Data:

9516309.3

9 August 1995 (09.08.95)

GB

(71) Applicant (for all designated States except US): THE UNIVERSITY OF SHEFFIELD [GB/GB]; Western Bank, Sheffield S10 2UH (GB).

(72) Inventor; and

(75) Inventor/Applicant (for US only): AGGARWAL, Varinder, Kumar [GB/GB]; The University of Sheffield, Dept. of Chemistry, Dainton Building, Sheffield S2 7HF (GB).

(74) Agent: RUTTER, Keith; SmithKline Beecham, Corporate Intellectual Property, SB House, Great West Road, Brentford, Middlesex TW8 9BD (GB).

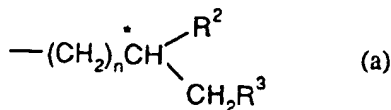
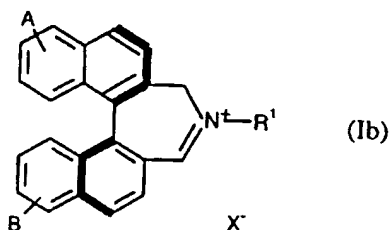
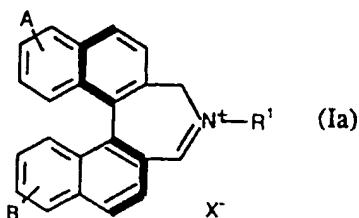
(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: DINAPHTAZEPINIUM SALTS USEFUL AS ENANTIOSELECTIVE EPOXIDATION CATALYSTS



(57) Abstract

A compound of formula (Ia) or (Ib), wherein A and B each independently represents hydrogen or one, two or three naphthylidene substituents, which substituents are selected from C₁₋₆ alkyl, C₁₋₆ alkoxy, aryl, aryloxy, silyl and silyloxy; R¹ represents phenyl, C₁₋₆ alkyl, phenyl C₁₋₆ alkyl or a moiety of formula (a); wherein R² represents C₁₋₆ alkyl, phenyl or benzyl, R³ represents H or OR⁴, wherein R⁴ is C₁₋₆ alkyl or C₁₋₆ alkylsilyl and n is zero or an integer 1 or 2; and X is a counter ion; a process for the preparation of such compounds and the use of such compounds for enantioselectively epoxidising a prochiral olefin.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LI	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

DINAPHTAZEPINIUM SALTS USEFUL AS ENANTIOSELECTIVE EPOXIDATION CATALYSTS

This invention relates to novel compounds and the use of such compounds as catalysts in oxygen transfer reactions.

5 The catalytic asymmetric epoxidation of alkenes using chiral catalysts, in particular the salen manganese complexes of Jacobsen *et al* (International Patent Application, Publication Number WO/91/14694), is now well established methodology in asymmetric synthesis. The importance of these catalytic systems stems in the main from the versatility of application of the asymmetric
10 epoxidation reaction itself. This versatility is due to the many and varied nucleophiles which can be used to open the substrate epoxide providing a concomitantly varied range of enantiomerically enriched products which are increasingly required for use for the manufacture of biologically important compounds such as pesticides, herbicides and pharmaceuticals.

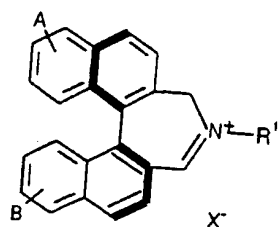
15 In addition to organo-transition metal based catalysts, such as the Jacobsen catalysts purely organic asymmetric catalysts are also known. Thus Hanquet *et al* (Tetrahedron Letters, Vol. 34, no.45, pp7271-7274) have demonstrated that the oxaziridinium salt (1S, 2R, 3R, 4S)-N-methyl-1,2-oxido-3-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinolinium tetrafluoroborate catalyses the asymmetric
20 epoxidation of *trans*-stilbene and the asymmetric oxidation of methyl *p*-tolyl sulphide to the corresponding sulfoxide. The oxaziridinium salts are prepared *in situ* from a catalytic amount of an iminium salt and oxone (Hanquet *et al* C.R.Acad Sci., Paris, 1991, 313, SII, pp625-628).

25 Unlike the salen manganese complexes and other organo-transition metal based catalysts, the oxaziridinium catalysts do not function by means of radical intermediates. They may therefore be used with a wider range of alkene substrates as there is no requirement for π -stabilising groups on the alkene (to stabilise incipient radicals). Also, the oxidation reactions of the oxaziridinium catalysts are stereospecific in the sense that *cis* alkenes give *cis* epoxides and *trans*
30 alkenes give *trans* epoxides. To date however, despite these advantages, the oxaziridinium catalysts have not provided oxidation systems for use on an industrial scale.

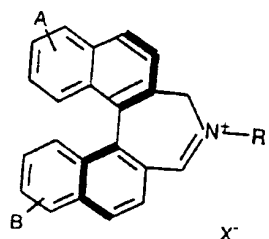
It has now been discovered that a novel series of oxaziridium salts show much promise in the catalytic asymmetric epoxidation of alkenes. The catalytic

reaction employed is simple and robust enabling the use of readily available and cheap reagents as well as environmentally safe solvents.

Accordingly, in a first aspect, the invention provides a compound of formula (Ia) or (Ib):

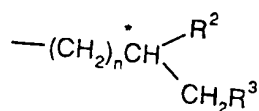


(Ia)



(Ib)

wherein A and B each independently represents hydrogen or one, two or three naphthylidene substituents, which substituents are selected from C₁₋₆ alkyl, C₁₋₆ alkoxy, aryl, aryloxy, silyl and silyloxy;
R¹ represents phenyl, C₁₋₆ alkyl, phenyl C₁₋₆ alkyl or a moiety of formula (a):



wherein R² represents C₁₋₆ alkyl, phenyl or benzyl, R³ represents H or OR⁴ wherein R⁴ is C₁₋₆ alkyl or C₁₋₆ alkylsilyl and n is zero or an integer 1 or 2; and

X is a counter ion.

Suitably, A represents hydrogen.

Suitably, B represents hydrogen.

Examples of R¹ when it represents C₁₋₆ alkyl are methyl and ethyl groups.

An example of R¹ is benzyl.

Suitably, R² represents C₁₋₆ alkyl.

Suitably, R³ represents C₁₋₆ alkyl.

Preferably, R¹ represents C₁₋₆ alkyl.

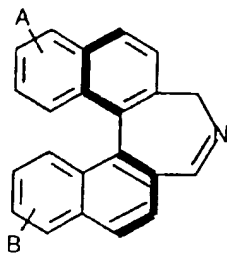
Values for the counter ion X⁻ include BF₄⁻, Cl⁻, Br⁻, I⁻, ClO₄⁻ and PF₆⁻.

A preferred value for the counter ion X⁻ is BF₄⁻.

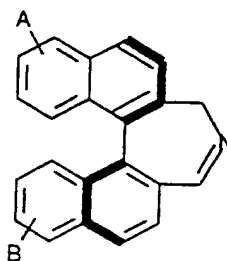
A suitable aryl group is a phenyl group.

As used herein, alkyl groups, whether present alone or as part of other groups such as alkoxy or aralkyl groups, are alkyl groups having straight or branched carbon chains, containing 1 to 6 carbon atoms, e.g. methyl, ethyl, n-propyl, iso-propyl, n-butyl, isobutyl or tert-butyl groups.

The compounds of formula (Ia) and (Ib) may be prepared by reacting, as appropriate, a compound of formula (IIa) or (IIb):



(IIa)



(IIb)

wherein A and B are as defined in relation to formula (I), with an alkylating agent of formula (III):



(III)

wherein R^1 is as defined in relation to formula (I) and L^1 is a leaving group or atom; and thereafter salting the compound produced with a source of counter ion X^- .

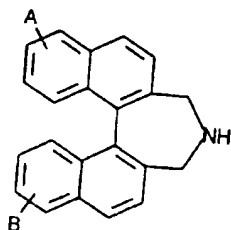
L^1 usually represents halide, such as bromide or iodide, tosyl, or mesyl.

The reaction between the compounds of formulae (II) and (III) may be carried out with or without a solvent; when using a solvent it is suitably an organic solvent, generally an inert organic solvent such as methylene dichloride, at a low to elevated temperature such as a temperature in the range of from 0 to 100°C, conveniently at ambient temperature; preferably the reaction is carried out under anhydrous conditions; preferably the reaction is carried out in an inert atmosphere, for example under nitrogen.

The salting reaction with the source of counter ion X^- may be carried out using any conventional procedure but is usually effected in the solvent used in the reaction, at ambient temperature.

The source of counter ion X^- may be any conventional source such as an appropriate metal salt and especially a silver salt, conveniently however alkylating agent (III) is also the source of counter ion X^- ; for example when preparing compounds of formula (Ia) or (Ib) wherein R^1 is C_{1-6} alkyl and X^- is BF_4^- , the compound of formula (II) is a compound $(R^{1a})_3OBF_4$, wherein R^{1a} is C_{1-6} alkyl, especially methyl.

The compounds of formula (IIa) and (IIb) may be prepared by oxidation of a chiral amine of formula (IV):



(IV)

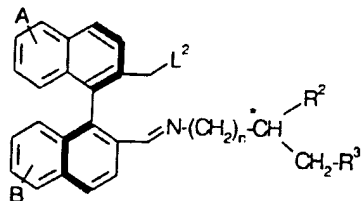
wherein A and B are as defined in relation to formula (I), suitably using potassium permanganate as oxidant in the method of Fleischhacker *et al*, monatschem. 1989 120 765.

The chiral compounds of formula (IV) may be prepared from the racemic compound of formula (IV) using conventional resolution methods, for example, the method disclosed by Hawkins and Fu in Journal of Organic Chemistry 1986, 51, 2820-2822.

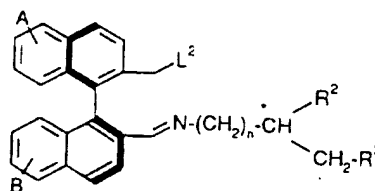
The compounds of formula (III) are known compounds or they may be prepared using methods analogous to those used to prepare known compounds, for example the methods disclosed by W. S. Johnson *et al*, Journal of American Chemical Society, 1963, 85, 1409.

The compounds of formula (IV) are known compound or they are prepared using methods analogous to those used to prepare known compounds, for example the methods disclosed by Hawkins and Fu *ibidem*.

The compounds of formula (Ia) and (Ib) wherein R^1 represents a moiety of the above defined formula (a), may be prepared, as appropriate, by cyclising a compound of formula (Va) or (Vb):



(Va)



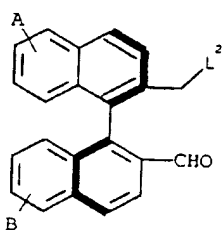
(Vb)

- 5 wherein A, B, R², R³ and n are as defined in relation to formula (I) and L² represents a leaving group; and thereafter salting the compound produced with a source of counter ion X⁻.

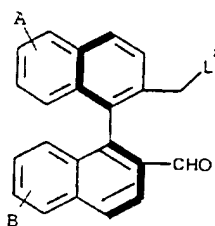
The cyclisation reaction of the compounds of formula (Va) and (Vb) may be carried out in an suitable organic solvent, usually an aprotic solvent such as acetone, at ambient or an elevated temperature, conveniently at the reflux temperature of the solvent.

The salting reaction with the source of counter ion X⁻ may be carried out using any conventional procedure but is usually effected in the solvent used in the cyclisation reaction, at ambient temperature. The source of counter ion X⁻ may be any conventional source such as an appropriate metal salt, for example when X⁻ is BF₄⁻ a suitable source is an alkali metal borotetrafluoride, such as sodium tetrafluoroborate or silver tetrafluoroborate.

The compounds of formula (Va) and (Vb) may be prepared by reacting, as appropriate, a compound of formula (VIa) or (VIb):

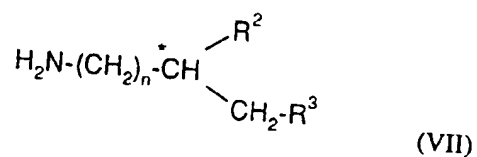


(VIa)



(VIb)

wherein A, B and L² are as defined in relation to formula (Va), with a compound of formula (VII):

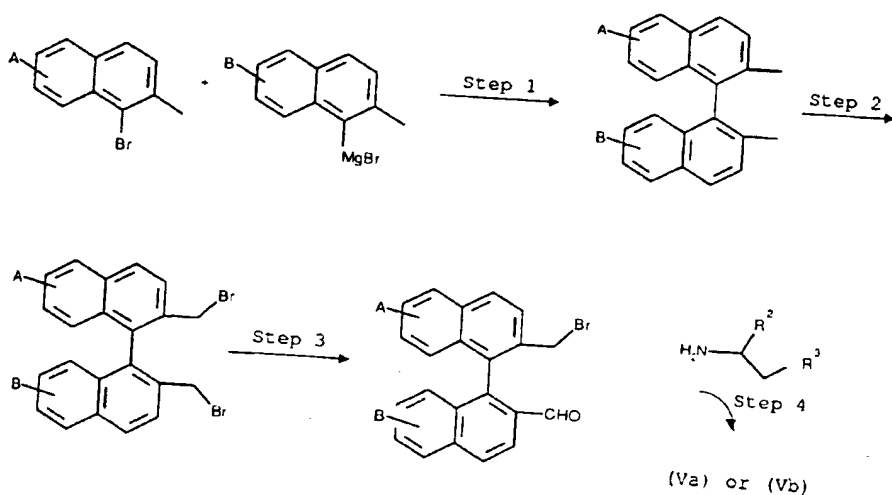


wherein R², R³ and n are as defined in relation to formula (I).

The reaction between the compound of formula (VIa) or (VIb) and the compound of formula (VII) may be carried out using any suitable organic solvent, generally an aprotic solvent such as tetrahydrofuran, usually at a low or medium elevated temperature such as a temperature in the range of from -78 to 50°C.

The compounds of formula (VII) are known compound or they may be prepared using methods analogous to those used to prepare known compounds, for example the methods disclosed by Evans *et al*, Organic Synthesis, Vol. 68, 1989, 77

The compounds of formula (VIa) and (VIb) may be prepared in accordance with methods illustrated below:



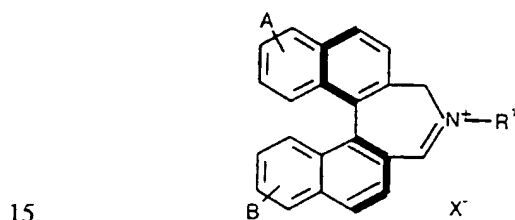
wherein A and B are as defined in relation to formula (I), the conditions of reaction and reagents used in for Steps 1 to 4 being those found in the following references:

Steps 1 and 2: N. Naigrot, J.P. Mazaleyrat, *Synthesis*, 1985, p 317.

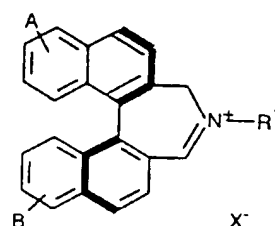
5 Step 3: H. B. Hass, M.L. Bender, *Org. Syn., Coll. Vol. 4*, 1963, 932.

Step 4: B. Bezas, L. Zervas, *JACS*, 1961, 83, 719.

As stated above the compounds of formula (I) are useful catalysts in the asymmetric epoxidation of alkenes. Accordingly, in a further aspect the invention provides a process for enantioselectively epoxidising a prochiral olefin
 10 such as 1-phenylcyclohexene, 1-methylcyclohexene, *trans*-stilbene and methylstilbene, which process comprises reacting the prochiral olefin with a nucleophilic oxidising agent in the presence of a catalyst, characterised in that the catalyst is a compound of formula (Ia) or (Ib):



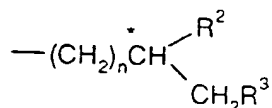
(Ia)



(Ib)

wherein A and B each independently represents hydrogen or one, two or three naphthylidene substituents, which substituents are selected from C₁₋₆ alkyl, C₁₋₆ alkoxy, aryl, aryloxy, silyl and silyloxy;

20 R¹ represents phenyl, C₁₋₆ alkyl, phenyl C₁₋₆ alkyl or a moiety of formula (a):



25 wherein R² represents C₁₋₆ alkyl, phenyl or benzyl;

R³ represents H or OR⁴ wherein R⁴ is C₁₋₆ alkyl or C₁₋₆ alkylsilyl and n is zero or an integer 1 or 2; and

X is a counter ion.

One suitable nucleophilic oxidising agent is provided by a mixture of oxone (KHSO_5) and NaHCO_3 .

5 The epoxidation reaction may be carried out using any suitable procedure wherein the prochiral olefin, the nucleophilic oxidising agent and the compound of formula (Ia) or (Ib) are allowed to react thereby providing the required epoxide.

The reaction is carried out in an organic solvent such as acetonitrile, dimethylsulphoxide, dimethylformamide or pyridine or in an organic solvent/water mixture such as aqueous acetonitrile.

10 Aqueous acetonitrile is a particularly apt reaction solvent when oxone/ NaHCO_3 is the nucleophilic oxidising agent.

The reaction is carried out at a low to medium-elevated temperature such as a temperature in the range of from -20 to 50°C , preferably at ambient temperature.

15 Suitably, the reaction is carried out at a neutral or alkaline pH such as in the range of from pH 7 to 14, preferably it is carried out in the range of from pH 8 to 10.

20 Suitably the molar ratio of the compound of formula (Ia) or (Ib) to the prochiral olefin is in the range of from 1 to 20mol %, preferably in the range of from 5 to 10 mol %.

The following preparation and examples illustrate the present invention.

Iminium Salt Catalysts

General Preparation Procedure:

To a solution of the required imine in CH_2Cl_2 was added the corresponding alkylating agent. The reaction was left to react at room temperature until completion. The solvent was then removed and the residue was precipitated out in ether to give the desired salt.

Example 1: (S)-(+)-5,5-Dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-methyl azepine Tetrafluoroborate

To a solution of (S)-imine from Preparation 1 (400mg, 1.36 mmol) in dry CH_2Cl_2 (10 ml) was added under N_2 , Me_3OBF_4 (222mg, 1.5 mmol) in one portion. The reaction was left to react at room temperature under N_2 for 24h. The solvent was removed and the residue was precipitated out in ether to give the desired salt (518 mg, 96%), $[\alpha]_{\text{D}}^{20} + 1070$ (c 1.1 in CH_2Cl_2); δ_{H} (250 MHz; CDCl_3) 4.05 (3H, s, CH_3), 4.6 (1 H, d, J 12.5 Hz, $\text{ArCH}'\text{H}$), 4.95 (1 H, d, J 12.5 Hz, ArCHH'), 7.0-8.25 (12 H, m, Ar-H), and 9.2 (1 H, s, $\text{CH}=\text{N}$); δ_{C} (62 MHz; CDCl_3) 48.76, 58.8, 125.29, 126.14, 126.78, 126.9, 127.12, 127.21, 127.5, 128.68, 129.54, 129.67, 130.12, 130.89, 131.41, 131.78, 131.93, 133.87, 135.29, 141.12, and 168.36; m/z (FAB) 308 ($\text{M}^+ - 87$, 100%) (Found 308.1448. $\text{C}_{23}\text{H}_{18}\text{N}$ requires 308.1439).

Example 2: (S)-(+)-5,5-Dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-methyl azepine iodide

A solution of (S)-imine from Preparation 1 (50 mg, 0.17 mmol) in iodomethane (2 ml) was stirred at room temperature, and very soon a yellow solid was formed in the reaction mixture. TLC of the reaction after 24 h showed only a small amount of starting material left. The remaining imine and excess of iodomethane were removed trituration with ether. After drying under high vacuum the desired compound was obtained as a yellow solid (72 mg, 97%); δ_{H} (250 MHz; CDCl_3) 4.25 (3 H, s, CH_3), 4.70 (1 H, d, J 13.1 Hz, $\text{ArCH}'\text{H}$), 4.85 (1 H, d, J 13.1 Hz, ArCHH'), 7.00-8.50 (12 H, m, Ar-H), and 10.50 (1 H, s, $\text{N}=\text{CH}$).

Example 3: (S)-(+)-5,5-Dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-methyl azepine perchlorate

A solution of AgClO_4 (34.3 mg, 0.17 mmol) in acetone (1 ml) was added to a solution of (S)-iminium salt from Example 2 (72 mg, 0.16 mmol) in CH_2Cl_2 (1 ml). The solid formed was filtered off and the filtrate was concentrated to give

the desired iminium salt which was precipitated from ether. After drying under high vacuum the desired compound was obtained as a yellow solid (60 mg, 90%), $[\alpha]_D^{20} + 769$ (c 1.09 in acetone); δ_H (250 MHz; $CDCl_3$) 4.15 (3 H, s, CH_3), 4.70 (1 H, d, J 13 Hz, $ArCHH'$), 4.80 (1 H, d, J 13 Hz, $ArCHH'$), 7.0-8.2 (12 H, m, $Ar-H$), and 9.35 (1 H, s, $N=CH$); δ_C (100 MHz; d_6 -acetone) 49.44, 59.19, 126.59, 126.64, 127.62, 127.85, 127.93, 128.03, 128.46, 129.58, 129.60, 130.01, 130.24, 130.26, 130.91, 131.76, 132.18, 132.40, 132.82, 134.83, 136.92, 141.86, and 169.98.

10 **Example 4: (R)-(-)-5,5-Dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-methyl azepine hexafluorophosphate**

A solution of $AgPF_6$ (40.7 mg, 0.16 mmol) in acetone (1 ml) was added to a solution of (R)-iminium salt from Example 2 (70 mg, 0.16 mmol) in CH_2Cl_2 (2 ml). The solid formed was filtered off and the filtrate was concentrated to give the desired iminium salt which was precipitated from ether. After drying under high vacuum the desired compound was obtained as a yellow solid (65 mg, 92%), $[\alpha]_D^{20} - 778$ (c 1.25 in acetone); δ_H (250 MHz; $CDCl_3$) 4.09 (3 H, s, CH_3), 4.64 (1 H, d, J 13 Hz, $ArCHH'$), 4.89 (1 H, d, J 13 Hz, $ArCHH'$), 7.00-8.25 (12 H, m, $Ar-H$), and 9.12 (1 H, s, $N=CH$); δ_C (100 MHz; CD_2Cl_2) 49.22, 59.60, 125.17, 125.95, 126.67, 127.42, 127.52, 127.82, 128.18, 129.02, 129.07, 129.96, 130.24, 130.97, 131.42, 131.94, 132.37, 132.44, 134.37, 135.02, 135.92, 142.19, and 168.56.

25 **Example 5: (S)-(+)-5,5-Dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-ethyl azepine Iodide**

A solution of (S)-imine from Preparation 1 (50 mg, 0.17 mmol) in iodoethane (2 ml) was stirred at room temperature, a yellow solid was soon formed in the reaction mixture. TLC of the reaction after 24 h showed that only a small amount of starting material was left. The remaining imine and excess iodoethane were removed by trituration with ether. After drying under high vacuum the desired product was obtained as a yellow solid (60 mg, 98%), m.p. $>200^\circ C$ (dec.), $[\alpha]_D^{20} + 878$ (c 0.41 in CH_2Cl_2); δ_H (250 MHz; $CDCl_3$) 1.51 (3 H, t, J 7 Hz, CH_3), 4.45-4.75 (2 H, m, CH_2CH_3), 4.6 (1 H, d, J 12.5 Hz, $ArCHH'$), 4.95 (1 H, d, J 12.5 Hz, $ArCHH'$), 7.00-8.60 (12 H, m, $Ar-H$), and 10.60 (1 H, s, $N=CH$); δ_C (100 MHz; CD_2Cl_2) 14.30, 57.75, 57.86, 125.21, 127.09, 127.42, 127.62, 127.68, 127.89, 128.93, 129.04, 129.75, 129.84, 130.62, 131.72, 131.93, 132.04, 132.45, 134.23, 135.41, 135.80, 141.95, and 168.23; m/z (FAB) 323 ($M^+ - 128$), 322 ($M^+ - 129$, 100%), and 308 ($M^+ - 141$); HRMS: m/z calc. 322.1604. $C_{24}H_{20}N$ ($M^+ - 127$) found 322.1596.

5 **Example 6: (R)-(-)-5,5-Dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-ethyl azepine Tetrafluoroborate**

A solution of AgBF₄ (40 mg, 0.2 mmol) in acetone (1 ml) was added to a solution of the (R)-iminium salt from Example 5 (76 mg, 0.17 mmol) in CH₂Cl₂ (2 ml). The solid (AgI) formed was removed by filtration. The resulting foam, obtained by concentration of the filtrate, was triturated with ether to give the
10 desired product as a yellow gum (59 mg, 84%); [α]_D²⁰ - 832 (c 0.87 in acetone); δ_H (250 MHz; CD₂Cl₂) 1.50 (3 H, t, J 6.5 Hz, CH₃), 4.25 (2 H, q, J 6.5 Hz, CH₂CH₃), 4.53 (1 H, d, J 13 Hz, ArCH'H), 4.94 (1 H, d, J 13 Hz, ArCHH'), 6.9-8.15 (12 H, m, Ar-H), and 9.13 (1 H, s, N=CH); δ_C (100 MHz; CD₂Cl₂) 13.87, 57.49, 58.38, 125.46, 126.33, 126.88, 127.02, 127.10, 127.15, 127.86, 128.86,
15 128.97, 129.67, 129.97, 130.64, 131.60, 131.87, 132.01, 132.40, 134.25, 135.82, 141.86, and 167.90

Example 7: (S)-(+)-5,5-Dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-benzyl azepine Bromide

20 A solution of (S)-imine from Preparation 1 (50 mg, 0.17 mmol) in benzyl bromide (2 ml) was left to stir at room temperature for 2 days. TLC of the reaction showed a small amount of starting material left. Excess benzyl bromide was removed under vacuum and the residue was triturated with ether to remove the unreacted starting material and trace amounts of benzyl bromide. After
25 drying under high vacuum the desired compound was obtained as a yellow solid (75 mg, 95%), m.p. 150-152 °C (dec.), [α]_D²⁰ + 450 (c 1.48 in CH₂Cl₂); δ_H (250 MHz; CDCl₃) 4.45 (1 H, d, J 13.4 Hz, ArCH'H), 4.90 (1 H, d, J 13.4 Hz, ArCHH'), 5.80 (1 H, d, J 13.0 Hz, PhCH'H), 5.94 (1 H, d, J 13.0 Hz, PhCHH'), 6.75-8.6 (17 H, m, Ar-H), and 11.22 (1 H, s, N=CH); δ_C (100 MHz; CDCl₃)
30 56.55, 65.28, 124.68, 126.86, 126.94, 127.19, 127.44, 128.47, 128.65, 128.74, 128.97, 129.35, 129.49, 129.87, 130.19, 130.90, 131.03, 131.45, 131.60, 133.44, 135.34, 141.42, and 169.45; m/z (FAB) 385 (M⁺-79), 384 (M⁺-80, 100%); HRMS: m/z calc. 384.1745 C₂₉H₂₂N (M⁺-80) requires 384.1752.

35 **Example 8: (R)-(-)-5,5-Dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-benzyl azepine Tetrafluoroborate**

To a solution of (R)-bromide salt from Example 7 (prepared from 50 mg, 0.17 mmol of (R)-imine from Preparation 1) in CH₂Cl₂ (2 ml) was added AgBF₄ (40 mg, 0.2 mmol). The solid (AgBr) formed was separated and the filtrate

concentrated. The resulting foam was triturated with ether to give the desired product as a yellow gum (48 mg, 60%); $[\alpha]_D^{20}$ - 637 (c 0.6 in acetone); δ_H (250 MHz; $CDCl_3$) 4.55 (1 H, d, J 12.5 Hz, $ArCH'H$), 4.95 (1 H, d, J 12.5 Hz, $ArCH'H$), 5.48 (1 H, d, J 14 Hz, $PhCH'H$), 5.58 (1 H, d, J 13 Hz, $PhCH'H$), 6.65-8.16 (17 H, m, Ar-H), and 9.55 (1 H, s, $N=CH$); δ_C (100 MHz; $CDCl_3$) 56.54, 66.12, 124.71, 126.60, 126.63, 126.92, 127.14, 127.51, 128.50, 128.66, 129.43, 129.47, 129.70, 130.01, 130.18, 130.29, 130.64, 130.95, 131.05, 131.45, 131.60, 133.46, 135.41, 135.44, 141.56, and 168.17.

10

Catalytic Epoxidation using Iminium Salt Catalysts

General Procedure

To a solution of alkene (0.5 mmol) in a mixture of acetonitrile (4.5 ml) and water (1-2 drops) were added first finely crushed $NaHCO_3$ (2 mmol) and oxone (0.5 mmol) then the catalyst (0.05 mmol or 0.025 mmol). The resulting yellow suspension was allowed to react at room temperature, under good stirring. The reaction was monitored using thin layer chromatography (TLC). Usually towards the end of the reaction the colour of the mixture changed from bright yellow to nearly colourless. Water was added to the reaction mixture followed by extraction into methylene dichloride. The organic extracts were combined and dried over anhydrous sodium sulphate. Concentration on a rotary evaporator gave a material which was purified (column chromatography) to give the desired epoxide.

25

Example 1: Preparation of Phenyl cyclohexene oxide

To a solution of phenyl cyclohexene (79mg, 0.5 mmol) in a mixture of acetonitrile (4.5 ml) and water (2 drops) were added first finely crushed $NaHCO_3$ (168 mg, 2mmol) and oxone (307 mg, 0.5 mmol) then the catalyst (0.05 mmol). The resulting yellow suspension was allowed to react at RT, under good stirring. TLC was used to follow the reaction which indicated that the reaction was finished in 2 h. Water (3 ml) was added to the reaction mixture followed by extraction into methylene dichloride. The organic extracts were combined and dried over anhydrous sodium sulphate. Concentration on a rotary evaporator gave a material which was purified on a column using 2% ethyl acetate : petrol

35

mixture as eluent to give the desired compound as a colourless oil. (72mg, 83% yield, 70% e.e).

The epoxidation of phenyl cyclohexene to phenyl cyclohexene oxide was then carried out using other catalysts of the invention. The results obtained are shown in Table 1

Table 1

Example No.	R ¹	X	Yield %	ee %
1	Me	BF ₄	83	70
3	Me	ClO ₄	54	74
4	Me	PF ₆	48	61
5	Et	I	55	78
6	Et	BF ₄	78	76
7	Bn	Br	71	74
8	Bn	BF ₄	78	73

Preparation 1: (R(-) and S(+)) 5,5-Dihydro-2H-dinaphth[2,1-c:1',2'-e]azepine

To a solution of (R)- or (S)-amine (295 mg, 1 mmol) (Journal of Organic Chemistry, 1986, 51, 2820-2822) in THF (5ml) was added KMnO₄ (648 mg, 4 mmol). The reaction was allowed to react at room temperature for 5 h before the solid was removed by filtration. Concentration of the filtrate followed by purification on column using ethyl acetate : petrol (1:1) as eluant gave the desired compound as a syrup (234 mg, 80%).

(S)- isomer, $[\alpha]_D^{20} +1363.7$, (c 1.19 in CH₂Cl₂);

(R)- isomer, $[\alpha]_D^{20} -1363.7$, (c 1.19 in CH₂Cl₂);

Both isomers: δ_H (250 MHz; CDCl₃) 3.95 (1 H, dd, J 2.2 Hz and 11 Hz,

ArCHH), 4.96 (1 H, d, J 11 Hz, ArCHH'), 7.0-8.1 (12 H, m, Ar-H), and 8.6 (1 H, d, J 2.2 Hz, CH=N); δ_C (62 MHz; CDCl₃) 55.90, 124.36, 125.27, 125.87, 126.05, 126.42, 126.69, 127.16, 127.49, 128.07, 128.25, 128.44, 129.18, 130.49,

131.70, 132.08, 132.34, 132.99, 135.04, 136.99, 140.96, and 162.47; m/z (FAB)
294 ($M^{+}+1$, 100%), 154 ($M^{+}-139$), and 136 ($M^{+}-157$) (Found
294.1275. $C_{22}H_{16}N$ requires 294.1283).

5

10

15

20

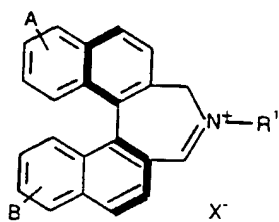
25

30

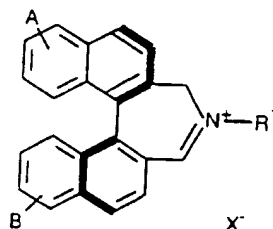
35

Claims:

1. A compound of formula (Ia) or (Ib):

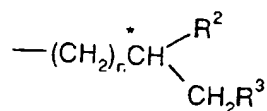


(Ia)



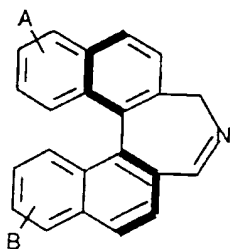
(Ib)

- wherein A and B each independently represents hydrogen or one, two or three naphthylidene substituents, which substituents are selected from C₁₋₆ alkyl, C₁₋₆ alkoxy, aryl, aryloxy, silyl and silyloxy;
 10 R¹ represents phenyl, C₁₋₆ alkyl, phenyl C₁₋₆ alkyl or a moiety of formula (a):

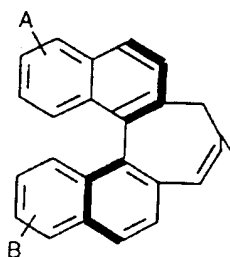


- 15 wherein R² represents C₁₋₆ alkyl, phenyl or benzyl, R³ represents H or OR⁴
 wherein R⁴ is C₁₋₆ alkyl or C₁₋₆ alkylsilyl and n is zero or an integer 1 or 2;
 and
 X is a counter ion.
 2. A compound according to claim 1, wherein A represents hydrogen and B
 20 represents hydrogen.
 3. A compound according to claim 1 or claim 2, wherein R¹ represents C₁₋₆ alkyl
 25 4. A compound according to any one of claims 1 to 3, wherein R¹ represents C₁₋₆ alkyl.
 5. A compound according to any one of claims 1 to 4, wherein R¹ represents methyl or ethyl.

6. A compound according to any one of claims 1 to 5, wherein counter ion X^- is selected from the list consisting of: BF_4^- , Cl^- , Br^- , I^- , ClO_4^- and PF_6^- .
7. A compound according to any one of claims 1 to 6, wherein counter ion X^- is BF_4^- .
8. A compound according to claim 1, selected from the list consisting of:
 (S)-(+)-5,5-dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-methyl azepine tetrafluoroborate;
 10 (S)-(+)-5,5-dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-methyl azepine iodide;
 (S)-(+)-5,5-dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-methyl azepine perchlorate;
 (R)-(-)-5,5-dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-methyl azepine hexfluorophosphate;
 (S)-(+)-5,5-dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-ethyl azepine iodide;
 15 (R)-(-)-5,5-dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-ethyl azepine tetrafluoroborate;
 (S)-(+)-5,5-dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-benzyl azepine bromide; and
 (R)-(-)-5,5-dihydro-2H-dinaphth[2,1-c:1',2'-e]-N-benzyl azepine tetrafluoroborate.
9. A process for the preparation of the compounds of formula (Ia) and (Ib) which process comprises reacting, as appropriate, a compound of formula (IIa) or (IIb):



(IIa)



(IIb)

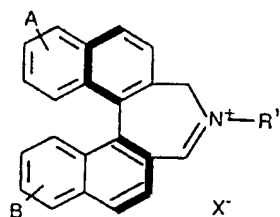
- 25 wherein A and B are as defined in relation to formula (I), with an alkylating agent of formula (III):



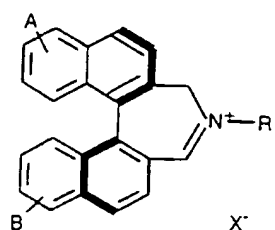
(III)

wherein R^1 is as defined in relation to formula (I) and L^1 is a leaving group or atom; and thereafter salting the compound produced with a source of counter ion X^- .

10. A process for enantioselectively epoxidising a prochiral olefin which process comprises reacting the prochiral olefin with a nucleophilic oxidising agent in the presence of a catalyst, characterised in that the catalyst is a compound of formula (Ia) or (Ib):



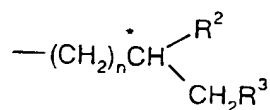
(Ia)



(Ib)

wherein A and B each independently represents hydrogen or one, two or three naphthylidene substituents, which substituents are selected from C_{1-6} alkyl, C_{1-6} alkoxy, aryl, aryloxy, silyl and silyloxy;

- 15 R^1 represents phenyl, C_{1-6} alkyl, phenyl C_{1-6} alkyl or a moiety of formula (a):



wherein R^2 represents C_{1-6} alkyl, phenyl or benzyl;

- 20 R^3 represents H or OR^4 wherein R^4 is C_{1-6} alkyl or C_{1-6} alkylsilyl and n is zero or an integer 1 or 2; and X is a counter ion.

25

30

INTERNATIONAL SEARCH REPORT

Inter national Application
PCT/EP 96/03551

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D223/14 C07F7/08 C07D301/03 C07B53/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TETRAHEDRON LETTERS, vol. 34, no. 45, 1993, OXFORD GB, pages 7271-4, XP002020018 L. BOHE ET AL.: "The stereospecific synthesis of a new chiral oxaziridinium salt" cited in the application see the whole document	1-10
Y	--- TETRAHEDRON LETTERS, vol. 24, no. 12, 1983, OXFORD GB, pages 1243-6, XP002020019 J.P. MAZALEYRAT: "Méthode simple de synthèse d'agents de transfert chiraux par action d'un agent alkylant à squelette binaphtyle-1,1" see the whole document --- -/-	1-10

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *Z* document member of the same patent family

Date of the actual completion of the international search

2 December 1996

Date of mailing of the international search report

10.12.1996

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Allard, M

INTERNATIONAL SEARCH REPORT

Inter. no. Application No.

PCT/EP 96/03551

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
----------	--	-----------------------

Y	US 5 360 568 A (S.A. MADISON ET AL.) 1 November 1994 see the whole document ---	1-10
P,X	CHEMICAL COMMUNICATIONS, no. 2, January 1996, CAMBRIDGE GB, pages 191-2, XP002020020 V. K. AGGARWAL ET AL.: "Catalytic asymmetric synthesis of epoxides mediated by chiral iminium salts" see the whole document -----	1-10

INTERNATIONAL SEARCH REPORT

Information on family members

International Application

PCT/EP 96/03551

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-5360568	01-11-94	AU-A- 8060994	29-05-95
		WO-A- 9513352	18-05-95
		EP-A- 0728182	28-08-96
		US-A- 5482515	09-01-96
		US-A- 5550256	27-08-96
		ZA-A- 9408978	13-05-96